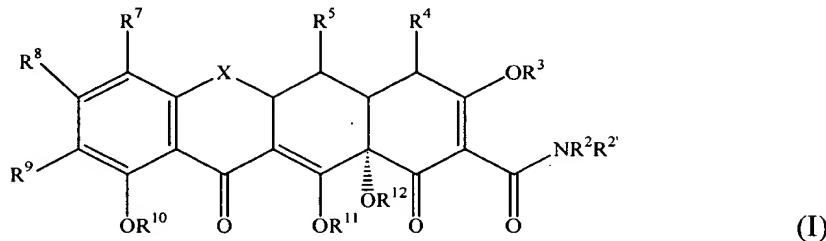


## CLAIMS

1. A substituted tetracycline compound of Formula I:

5



wherein:

X is  $\text{CHC}(\text{R}^{13}\text{Y})\text{Y}$ ,  $\text{CR}^6\text{R}^6$ ,  $\text{C}=\text{CR}^6\text{R}^6$ , S,  $\text{NR}^6$ , or O;

10  $\text{R}^2$ ,  $\text{R}^2'$ ,  $\text{R}^4'$ , and  $\text{R}^{4''}$  are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$\text{R}^4$  is  $\text{NR}^4\text{R}^{4''}$ , alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

$\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$  and  $\text{R}^{12}$  are each hydrogen or a pro-drug moiety;

$\text{R}^5$  is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyle, aryl,

15 heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

$\text{R}^6$  and  $\text{R}^{6'}$  are each independently hydrogen, methylene, absent,

hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

20  $\text{R}^7$  is nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, or  $-(\text{CH}_2)_{0-3}\text{NR}^{7c}\text{C}(=\dot{\text{W}}')\text{WR}^{7a}$ ;

$\text{R}^9$  is hydrogen, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, thionitroso(e.g.,  $-\text{N}=\text{S}$ ), or  $-(\text{CH}_2)_{0-3}\text{NR}^{9c}\text{C}(=\text{Z}')\text{ZR}^{9a}$ ;

25 Z is  $\text{CR}^{9d}\text{R}^{9e}$ , S,  $\text{NR}^{9b}$  or O;

$\text{Z}'$  is O, S, or  $\text{NR}^{9f}$ ;

W is  $\text{CR}^{7d}\text{R}^{7e}$ , S,  $\text{NR}^{7b}$  or O;

$\text{W}'$  is O,  $\text{NR}^{7f}$  S;

$\text{R}^{7a}$ ,  $\text{R}^{7b}$ ,  $\text{R}^{7c}$ ,  $\text{R}^{7d}$ ,  $\text{R}^{7e}$ ,  $\text{R}^{9a}$ ,  $\text{R}^{9b}$ ,  $\text{R}^{9c}$ ,  $\text{R}^{9d}$ , and  $\text{R}^{9e}$  are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$\text{R}^8$  is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R<sup>13</sup> is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl, and pharmaceutically acceptable salts thereof.

2. The tetracycline compound of claim 1, wherein R<sup>4</sup> is NR<sup>4'</sup>R<sup>4''</sup>, X is CR<sup>6</sup>R<sup>6'</sup>; R<sup>2</sup>, R<sup>2'</sup>, R<sup>6</sup>, R<sup>6'</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> are each hydrogen; R<sup>4'</sup> and R<sup>4''</sup> are lower alkyl; and R<sup>5</sup> is hydroxy or hydrogen.

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3. The tetracycline compound of claim 2, wherein R<sup>4'</sup> and R<sup>4''</sup> are each methyl and R<sup>5</sup> is hydrogen.

4. The tetracycline compound of any one of claims 1-3, wherein R<sup>7</sup> is aryl.

5. The tetracycline compound of claim 4, wherein R<sup>7</sup> is substituted or unsubstituted phenyl.

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6. The tetracycline compound of claim 5, wherein said phenyl is substituted with a substituent selected from the group consisting of alkyl, alkenyl, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, amino, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl and heteroaryl.

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7. The tetracycline compound of claim 6, wherein said substituent is substituted or unsubstituted alkyl.

8. The tetracycline compound of claim 5, wherein said alkyl is substituted with a heterocycle.

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9. The tetracycline compound of claim 8, wherein said heterocycle is morpholine, piperidine, or pyrrolidine.

10. The tetracycline compound of claim 5, wherein said phenyl is substituted with an amino group.

11. The tetracycline compound of claim 10, wherein said amino group is substituted with one or more substituent selected from the group consisting of alkyl, alkenyl, alkynyl, carbonyl, alkoxy and aryl group.

12. The tetracycline compound of claim 11, wherein said amino group is substituted with an alkoxy group.

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13. The tetracycline compound of claim 11, wherein said amino group is substituted with a substituted or unsubstituted phenyl group.

14. The tetracycline compound of claim 13, wherein said substituted phenyl is substituted with a halogen.

15

15. The tetracycline compound of claim 13, wherein said substituted phenyl amino group is substituted with a second substituted amino group.

20

16. The tetracycline compound of claim 15, wherein said second substituted amino group is substituted or unsubstituted aryl.

17. The tetracycline compound of claim 16, wherein said second substituted amino group is a second substituted phenyl.

25

18. The tetracycline compound of claim 5, wherein said phenyl group is substituted with alkoxy.

19. The tetracycline compound of claim 5, wherein said phenyl group is substituted with an alkoxycarbonylamino group.

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20. The tetracycline compound of claim 4, wherein said aryl group is substituted or unsubstituted naphthyl.

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21. The tetracycline compound of claim 20, wherein said naphthyl group is substituted with one or more substituents selected from the group consisting of alkyl, alkenyl, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, carboxy, arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxycarbonyloxy,

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carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, amino, acylamino, amido, imino, sulfhydryl, 5 alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl and heteroaryl.

22. The tetracycline compound of claim 21, wherein said substituent is amino or formyl. 10

23. The tetracycline compound of claim 4, wherein R<sup>7</sup> is heteroaryl.

24. The tetracycline compound of claim 23, wherein said heteroaryl is selected from the group consisting of furanyl, imidazolyl, benzothiophenyl, 15 benzofuranyl, quinolinyl, isoquinolinyl, pyridinyl, pyrazolyl, benzodioxazolyl, benzoxazolyl, benzothiazolyl, benzoimidazolyl, methylenedioxypyphenyl, indolyl, thienyl, pyrimidyl, pyrazinyl, purinyl, pyrazolyl, oxazolyl, isooxazolyl, naphthridinyl, thiazolyl, isothiazolyl, and deazapurinyl.

20 25. The tetracycline compound of claim 24, wherein said heteroaryl is thiazolyl, thiophenyl, or furanyl.

26. The tetracycline compound of any one of claims 1-3, wherein R<sup>7</sup> is substituted or unsubstituted alkyl. 25

27. The tetracycline compound of claim 26, wherein said alkyl is a straight or branched chain.

28. The tetracycline compound of claim 27, wherein said alkyl is methyl, 30 ethyl, i-propyl, n-propyl, n-butyl, i-butyl, t-butyl, pentyl, or hexyl.

29. The tetracycline compound of claim 26, wherein said alkyl comprises a cycloalkyl.

35 30. The tetracycline compound of claim 29, wherein said cycloalkyl is cyclopentyl, cyclohexyl, cyclopropyl, or cyclobutyl.

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31. The tetracycline compound of claim 26, wherein said alkyl is substituted with one or more substituents selected from the group consisting of alkenyl, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, carboxy, arylcarbonyloxy, alkoxy carbonylamino, alkoxy carbonyloxy, aryloxycarbonyloxy, carboxylate,

5 alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxy carbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, amino, acylamino, amido, imino, sulphydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl,

10 sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl and heteroaryl.

32. The tetracycline compound of claim 31, wherein said alkyl is substituted with an amino, hydroxy, carboxy, carbonyl or aryl group.

15 33. The tetracycline compound of claim 32, wherein said aryl group is heteroaromatic.

34. The tetracycline compound of claim 33, wherein said heteroaromatic group is furanyl, imidazolyl, benzothiophenyl, benzofuranyl, quinolinyl, isoquinolinyl,

20 benzodioxazolyl, benzoxazolyl, benzothiazolyl, benzoimidazolyl, methylenedioxophenyl, indolyl, thienyl, pyridinyl, pyrazolyl, pyrimidyl, pyrazinyl, purinyl, pyrazolyl, oxazolyl, isooxazolyl, naphthridinyl, thiazolyl, isothiazolyl, and deazapurinyl.

25 35. The tetracycline compound of claim 34, wherein said heteroaromatic group is pyridinyl.

36. The tetracycline compound of claim 32, wherein said aryl group is substituted or unsubstituted phenyl.

30 37. The tetracycline compound of claim 36, wherein said phenyl group is substituted with sulfonamido or alkyl.

38. The tetracycline compound of claim 32, wherein said carbonyl group is

35 morpholinylcarbonyl.

39. The tetracycline compound of any one of claims 1-3, wherein R<sup>7</sup> is substituted or unsubstituted alkenyl.

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40. The tetracycline compound of claim 39, wherein said alkenyl group is substituted with one or more substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, carboxy, 5 arylcarbonyloxy, alkoxycarbonylamino, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, amino, acylamino, amido, imino, sulfhydryl, 10 alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl and heteroaryl.

41. The tetracycline compound of claim 40, wherein said alkenyl group is substituted with an aminocarbonyl or alkoxycarbonyl. 15

42. The tetracycline compound of claim 41, wherein said aminocarbonyl is dialkylaminocarbonyl.

43. The tetracycline compound of claim 40, wherein said alkenyl group is 20 substituted with one or more halogens.

44. The tetracycline compound of claim 40, wherein said alkenyl group is substituted with one or more hydroxy groups.

25 45. The tetracycline compound of claim 40, wherein said alkenyl group is substituted with a heteroaryl.

46. The tetracycline compound of claim 45, wherein said heteroaryl is selected from the group consisting of furanyl, imidazolyl, benzothiophenyl, 30 benzofuranyl, quinolinyl, isoquinolinyl, benzodioxazolyl, benzoxazolyl, benzothiazolyl, benzoimidazolyl, methylenedioxophenyl, indolyl, thienyl, pyridinyl, pyrazolyl, pyrimidyl, pyrazinyl, purinyl, pyrazolyl, oxazolyl, isooxazolyl, naphthridinyl, thiazolyl, isothiazolyl, and deazapurinyl.

35 47. The tetracycline compound of claim 46, wherein said heteroaryl is thiazolyl.

48. The tetracycline compound of claim 40, wherein said aryl substituent is substituted or unsubstituted phenyl.

49. The tetracycline compound of claim 48, wherein said substituted phenyl is substituted with one or more halogens, alkoxy, hydroxy, or alkyl groups.

50. The tetracycline compound of claim 49, wherein said substituted phenyl is substituted with one or more fluorines.

*SAC 10*  
51. The tetracycline compound of any one claims 1-3, wherein R<sup>7</sup> is substituted or unsubstituted alkynyl.

52. The tetracycline compound of claim 51, wherein said substituted alkynyl is substituted with an aryl.

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53. The tetracycline compound of claim 52, wherein said substituted alkynyl is substituted with substituted or unsubstituted phenyl.

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54. The tetracycline compound of claim 53, wherein said substituted phenyl is substituted with one or more substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, carboxy, alkylcarbonylamino, arylcarbonyloxy, alkoxy carbonylamino, alkoxy carbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, 25 arylalkylcarbonyl, alkenylcarbonyl, alkoxy carbonyl, silyl, aminocarbonyl, alkylthiocarbonyl, phosphate, aralkyl, phosphonato, phosphinato, cyano, amino, acylamino, amido, imino, sulfhydryl, alkylthio, sulfate, arylthio, thiocarboxylate, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, cyano, azido, heterocyclyl, alkylaryl, aryl and heteroaryl.

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55. The tetracycline compound of claim 54, wherein said phenyl is substituted with alkylcarbonylamino or sulphonamido.

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56. The tetracycline compound of claim 51, wherein said substituted alkynyl is substituted with a tetracycline moiety.

*SAC AS*  
57. The tetracycline compound of any one of claims 1-3, wherein R<sup>7</sup> is alkylcarbonyl amino.

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cont

58. carbonyl. The tetracycline compound of any one of claims 1-3, wherein R<sup>7</sup> is carbonyl.

5 59. The tetracycline compound of claim 58, wherein R<sup>7</sup> is substituted or unsubstituted alkyl carbonyl.

10 60. The tetracycline compound of claim 59, wherein said alkyl carbonyl is substituted with an aryl.

10 61. The tetracycline compound of claim 60, wherein said aryl substituent is heteroaryl.

15 62. The tetracycline compound of claim 61, wherein said heteroaryl substituent is pyridinyl.

15 63. The tetracycline compound of any one of claims 1-3, wherein R<sup>7</sup> is substituted or unsubstituted imino.

20 64. The tetracycline compound of any one of claims 1-3, wherein said substituted imino is substituted with an hydroxy or alkoxy group.

25 65. The tetracycline compound of any one of claims 1-3, wherein R<sup>7</sup> is NR<sup>7c</sup>(C=W')WR<sup>7a</sup>.

25 66. The tetracycline compound of claim 55, wherein R<sup>7c</sup> is hydrogen, W' is oxygen and W is oxygen.

30 67. The tetracycline compound of claim 65 or 66, wherein R<sup>7a</sup> is substituted or unsubstituted phenyl.

35 68. The tetracycline compound of claim 67, wherein said substituted phenyl is substituted with one or more substituents selected from the group consisting of alkyl, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, alkyloxycarbonyl, carboxy, alkylcarbonylamino, arylcarbonyloxy, alkoxy carbonylamino, alkoxy carbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminoacarbonyl, arylalkyl aminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aminoalkyl, arylalkylcarbonyl, alkenylcarbonyl, alkoxy carbonyl, silyl, aminocarbonyl,

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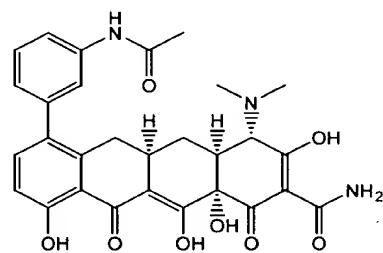
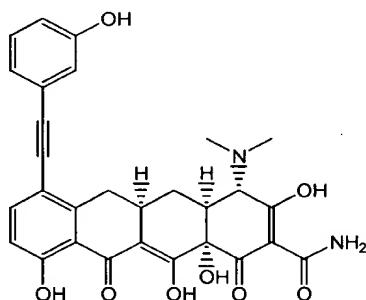
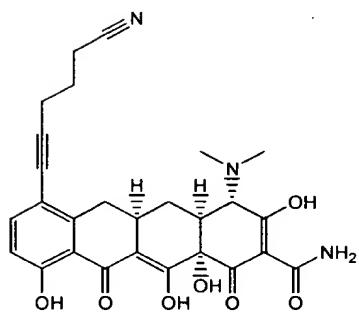
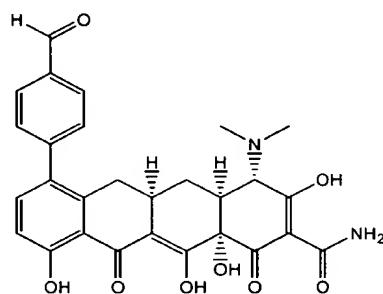
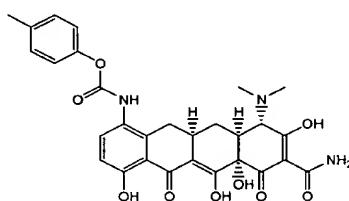
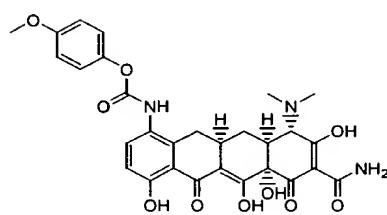
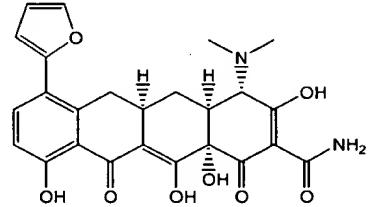
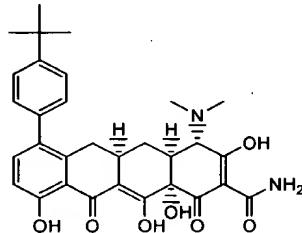
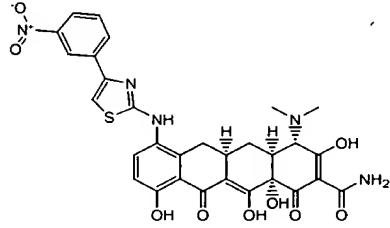
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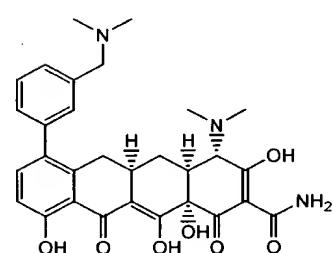
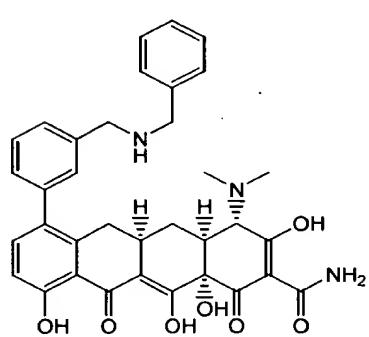
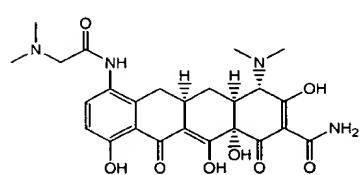
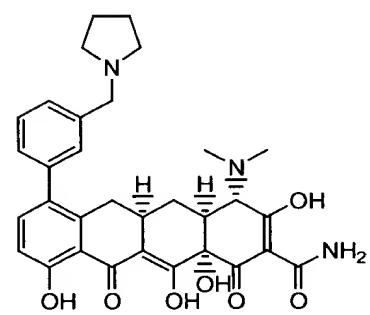
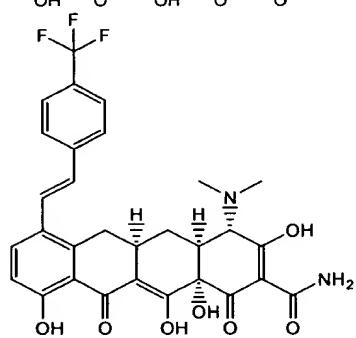
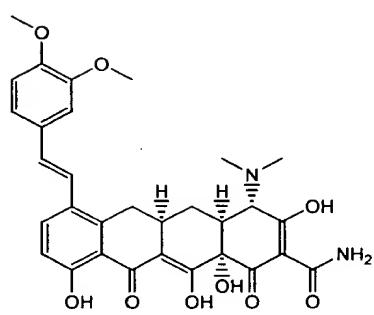
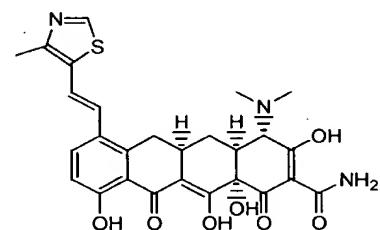
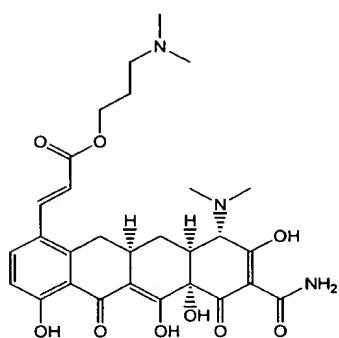
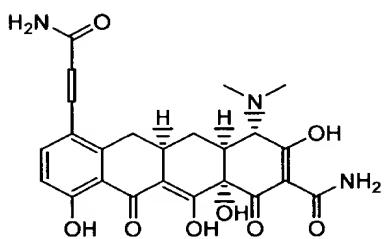
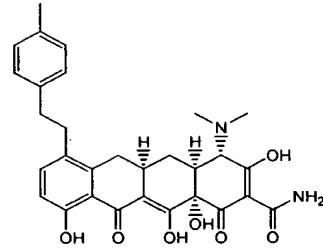
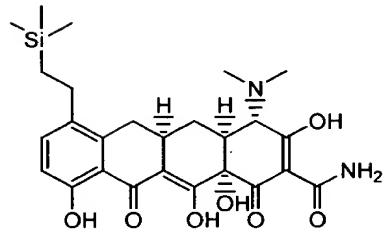
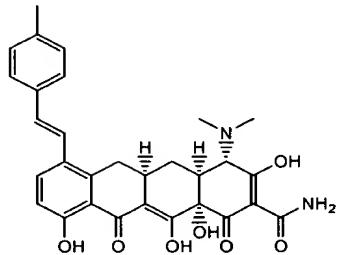
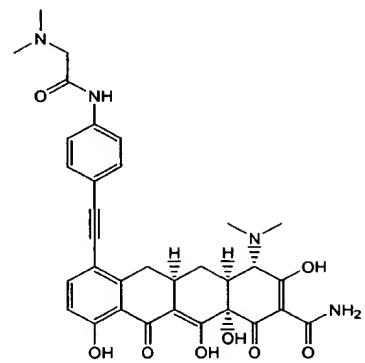
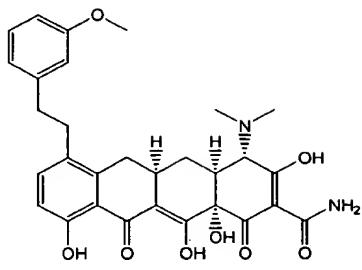
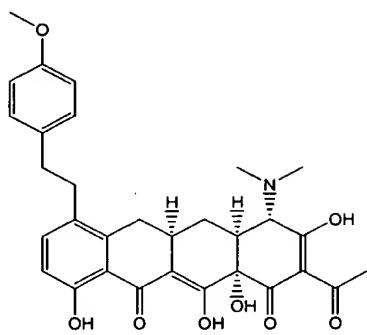
69. The tetracycline compound of claim 65 or 66 wherein R<sup>7a</sup> is alkyl.

70. The tetracycline compound of any one of claims 1-3, wherein R<sup>7</sup> is sulfonamido.

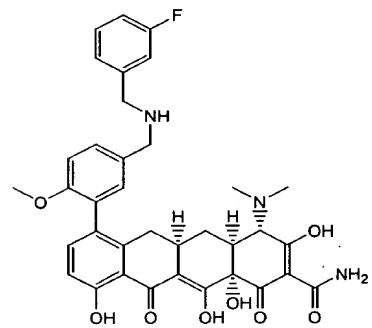
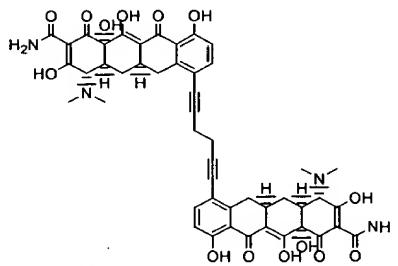
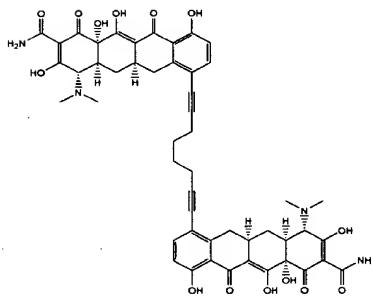
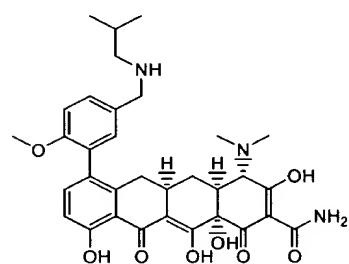
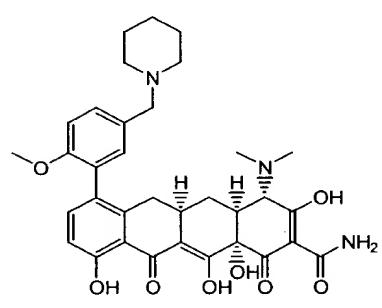
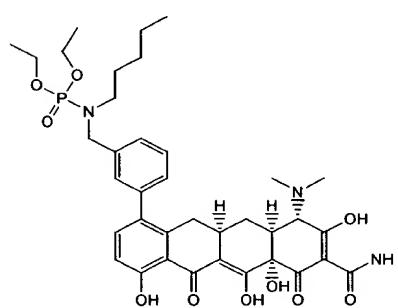
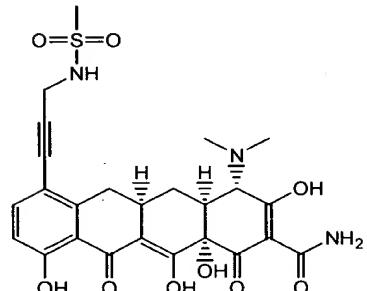
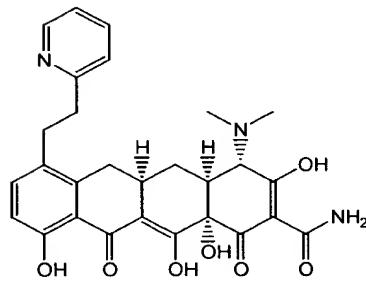
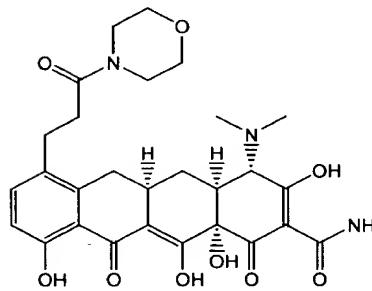
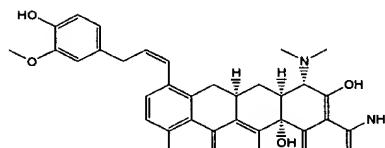
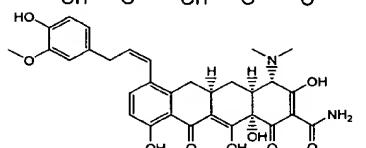
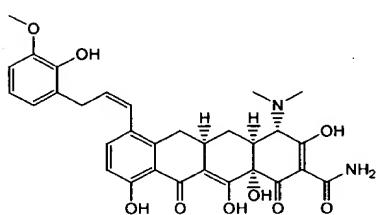
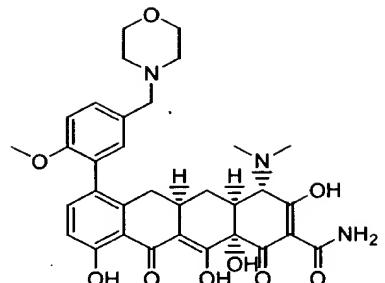
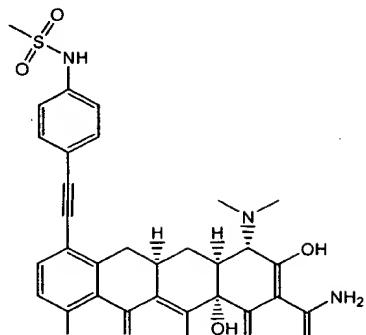
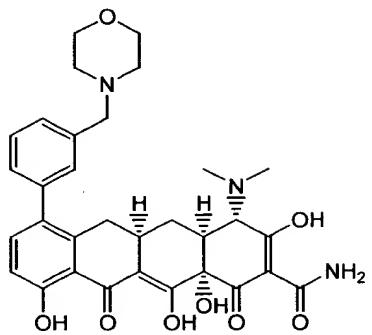
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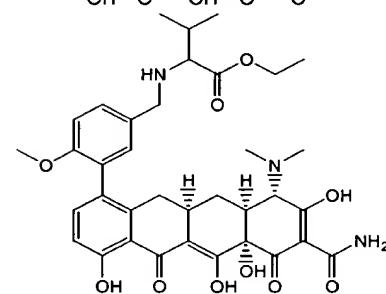
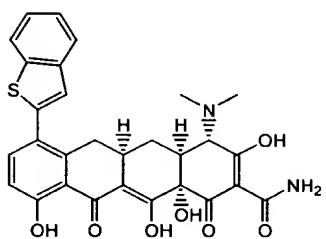
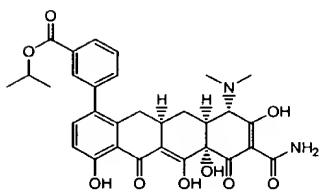
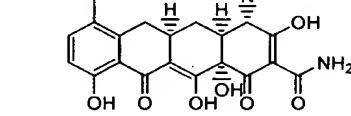
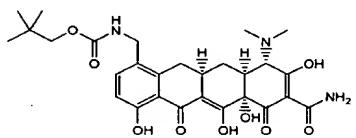
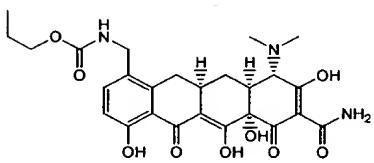
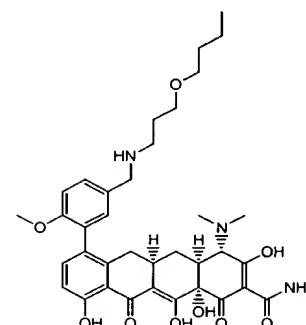
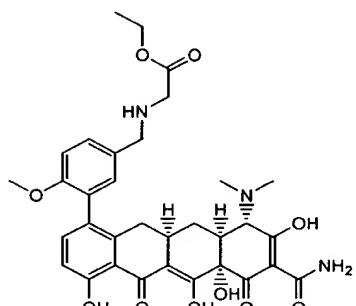
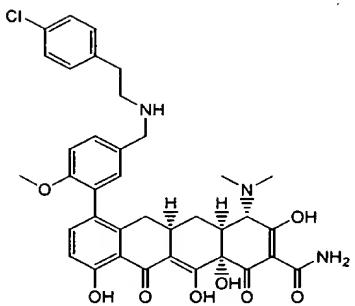
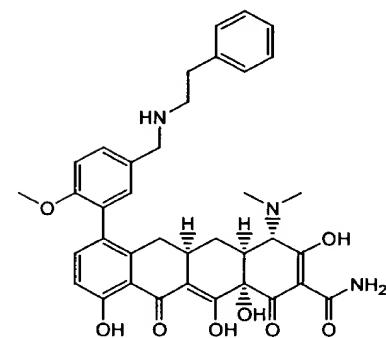
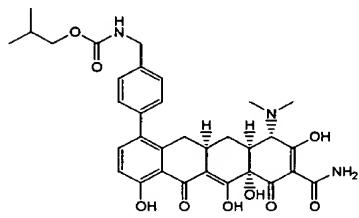
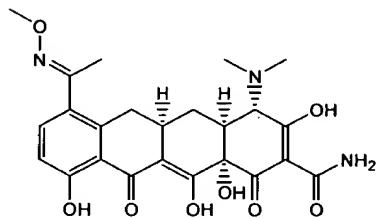
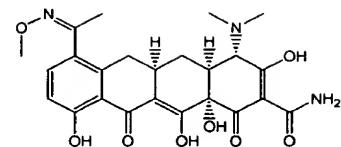
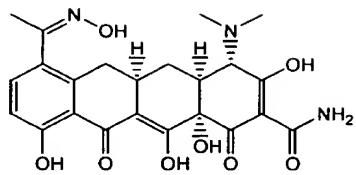
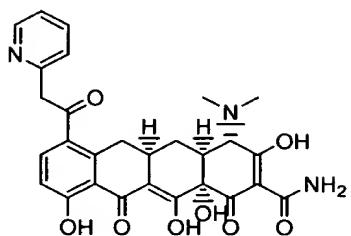
71. A tetracycline compound selected from the group consisting of:



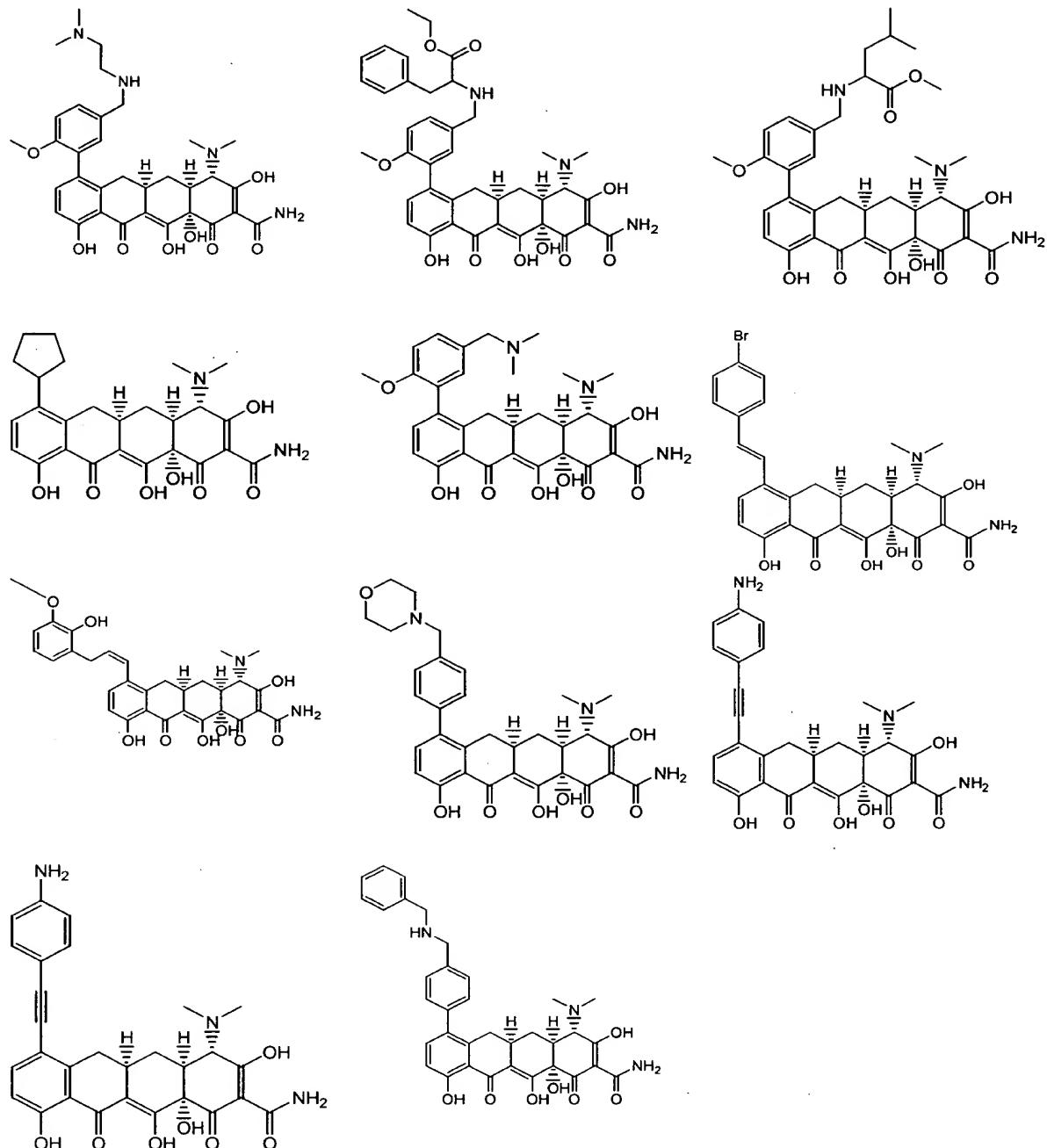


0 9 3 9 5 2 1 2 0 9 2 9 0 2 1



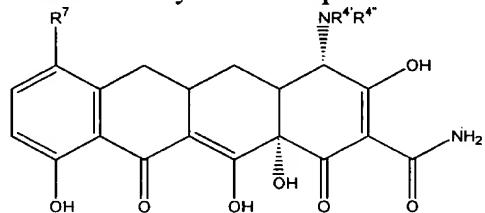


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and pharmaceutically acceptable salts, prodrugs and esters thereof.

72. A 7-substituted sancycline compound of the formula



(II)

5 wherein:

$R^{4'}$  and  $R^{4''}$  are each alkyl;



$R^7$  is a fused ring moiety of the formula where Q is C or a heteroatom; an acylfuran group; a tri-, tetra- or penta- halo substituted phenyl group; an aminomethylphenyl group; an acylaminomethyl group; an alkylesterphenyl group; an acylphenyl group; an acylalkynyl group; an acylalkoxyphenyl group; a methylphenyl group; a dimethylphenyl group; a carboxyphenyl group; a carboxyalkynyl group; a thiophene group; a halothiophene group; an alkoxy carbonylphenyl group; an alkoxyphenyl group; an alkoxyphenylalkynyl group; an alkoxypyridyl group; an alkylene pyridine group; a cyclopentyl or cyclopentenyl group; a cyclohexylalkynyl group; a cyclohexenylalkynyl group; a cyclohexenylhaloalkenyl group; a hydroxycyclohexylalkynyl group; a phenylalkynyl group; a phenylalkenyl group; an aminoalkynyl group; a cyclobutylalkenyl group; a pyridylalkynyl group; a pyridylalkenyl group; a nitrophenylalkynyl group; a nitrophenylalkenyl group; a cyanoalkynyl group; an alkynyl group; a cyanoalkenyl group; a cyanophenyl group; a dialkylamidoalkenyl group; a dialkylamidophenyl group; an aminophenylethyl group; an aminophenylethylnyl group; a haloethyl group; a halophenylalkynyl group; or an alkylester-substituted pentenyl group; and pharmaceutically acceptable salts, esters and prodrugs thereof.

20 73. The compound of claim 72, wherein said compound is 7-(2-benzofuran) sencycline, 7-(3-formylfuranyl) sencycline, 7-(2,3,4,5,6-pentafluorophenyl) sencycline, 7-(4-aminomethylphenyl) sencycline, 7-(4-formylaminomethylphenyl) sencycline, 7-(4-carboxyphenyl methylester) sencycline, 7-(2-carboxyphenyl ethylester) sencycline, 7-(4-tolyl) sencycline, 7-(3-formylphenyl) sencycline, 7-(4-formylphenyl) sencycline, 7-(3-acetylphenyl) sencycline, 7-(2-acetylphenyl) sencycline, 7-(3-acetylphenyl) sencycline, 7-(4-acetylphenyl) sencycline, 7-(3-formyl-6-methoxyphenyl) sencycline, 7-(4-methylphenyl) sencycline, 7-(3,5-dimethylphenyl) sencycline, 7-(3-carboxyphenyl) sencycline, 7-(carboxyethynyl) sencycline, 7-(3-thiophene) sencycline, 7-(3-methyl-2-thiophene) sencycline, 7-(3-methyl-5-thiophene) sencycline, 7-(3-chloro-2-thiophene) sencycline and 7-(4-chloro-2-thiophene) sencycline, 7-(2-ethoxycarbonylphenyl) sencycline, 7-(2-ethoxyphenyl) sencycline, 7-(3-ethoxyphenyl) sencycline, 7-(4-methoxyphenyl) sencycline, 7-(2,5-dimethoxyphenyl) sencycline, 7-(4-methoxyphenylethynyl) sencycline, 7-(4-methoxy-5-pyridyl) sencycline, 7-(cyclopentenyl) sencycline, 7-(cyclohexylethynyl) sencycline, 7-(1-ethynyl-1-cyclohexyl) sencycline, 7-(1-chlorovinyl-1-cyclohexyl) sencycline, 7-(1-ethynyl-1-

hydroxycyclohexyl) sencycline, 7-(phenylethynyl) sencycline, 7-(tolylethynyl) sencycline, 7-(4-methoxyphenylethynyl) sencycline, 7-(2-vinylpyridyl) sencycline, 7-(vinylphenyl) sencycline, 7-(dimethylaminoethynyl) sencycline, 7-(cyclobutylmethenyl) sencycline, 7-(2-pyridylethynyl) sencycline, 7-(3-pyridylethynyl) sencycline, 7-(4-pyridylethenyl) sencycline, 7-(cyano-1-pentynyl) sencycline, 7-(cyanohexenyl) sencycline, 7-(3-cyanophenyl) sencycline, 7-(4-cyanophenyl) sencycline, 7-(3-hydroxylphenylethynyl) sencycline, 7-(N,N-dimethylacrylamide) sencycline, 7-(dimethylamidoethenyl) sencycline, 7-(4-nitrophenylethynyl) sencycline, 7-(4-nitrostyryl) sencycline, 7-(ethynyl) sencycline, 7-(N,N-dimethylacrylamide) sencycline,

10 7-(3-dimethylamidophenyl) sencycline, 7-(4-methoxyphenyl) sencycline, 7-(4-aminophenylethyl) sencycline, 7-(2-chloroethenyl) sencycline, 7-(2-fluorophenylethenyl) sencycline, 7-(1-iodo-1,3-dicarboethoxy-1,3-butadiene) sencycline, or 7-(4-aminophenylvinyl) sencycline.

15 74. The compound of claim 1 or 71, wherein said compound is at least 75% free of positional isomers.

20 75. The compound of claim 74, wherein said compound is at least 80% free of positional isomers.

25 76. The compound of claim 75, wherein said compound is at least 85% free of positional isomers.

77. The compound of claim 76, wherein said compound is at least 90% free of  
25 positional isomers.

78. The compound of claim 77, wherein said compound is at least 95% free of positional isomers.

30 79. A method for treating a tetracycline responsive state in a subject, comprising administering to said subject a tetracycline compound of claims 1, 71, or 72, such that said subject is treated.

35 80. The method of claim 79, wherein said tetracycline responsive state is a bacterial infection.

81. The method of claim 80, wherein said bacterial infection is associated with *E. coli*.

82. The method of claim 80, wherein said bacterial infection is associated with *S. aureus*.

5 83. The method of claim 80, wherein said bacterial infection is associated with *E. faecalis*.

84. The method of claim 80, wherein said bacterial infection is resistant to other tetracycline antibiotics.

10 85. The method of claim 79, wherein said subject is a human.

86. The method of claim 79, wherein said tetracycline compound is administered with a pharmaceutically acceptable carrier.

15 87. A substituted tetracycline compound selected from the group listed in Table 2.

88. A pharmaceutical composition comprising a therapeutically effective amount of a tetracycline compound of claim 1, 71, 72, or 87 and a pharmaceutically acceptable carrier.

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